**Figure 1**

NR-LU-13 Heavy chain variable region sequences

GAG GTT CAG CTG CAG CAG TCT GGG GCA GAG CTT GTG AAG CCA GGG GCC TCA GTC	18
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val	
<u>CDR1</u>	
AGG TTG TCC TGC ACA GCT TCT GGC TTC AAC ATT AAA GAC ACC TAT ATG CAC TGG	36
Arg Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Met His Trp	
<u>CDR2</u>	
GTG ATA GAG AGG CCT GAA CAG GGC CTG GAG TGG ATT GGA AGG ATT GAT CCT GCG	54
Val Ile Glu Arg Pro Glu Gln Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Ala	
<u>CDR3</u>	
AAT GGT AAT ACT AAA TGT GAC CCG AAG TTC CAG GGC AAG GCC ACT ATA ACA GCA	72
Asn Gly Asn Thr Lys Cys Asp Pro Lys Phe Gln Gly Lys Ala Thr Ile Thr Ala	
GAC ACA TCC TCC AAC ACA GCC TAC CTG CAG CTC AGC AGC CTG ACA TCT GAG GAC	90
Asp Thr Ser Ser Asn Thr Ala Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp	
<u>CDR3</u>	
ACT GCC GTC TAT TAC TGT TCT AGA GAG GTC CTA ACT GGG ACG TGG TCT TTG GAC	108
Thr Ala Val Tyr Tyr Cys Ser Arg Glu Val Leu Thr Gly Thr Trp Ser Leu Asp	
TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA	120
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser	

NR-LU-13 Light chain variable region sequences

GAC ATC CAG ATG ATT CAG TCT CCA TCG TCC ATG TTT GCC TCT CTG GGA GAC AGA	18
Asp Ile Gln Met Ile Gln Ser Pro Ser Ser Met Phe Ala Ser Leu Gly Asp Arg	
<u>CDR1</u>	
GTC AGT CTC TCT TGT CGG GCT AGT CAG GGC ATT AGA GGT AAT TTA GAC TGG TAT	36
Val Ser Leu Ser Cys Arg Ala Ser Gln Gly Ile Arg Gly Asn Leu Asp Trp Tyr	
<u>CDR2</u>	
CAG CAG AAA CCA GGT GGA ACT ATT AAA CTC CTG ATC TAC TCC ACA TCC AAT TTA	54
Gln Gln Lys Pro Gly Gly Thr Ile Lys Leu Leu Ile Tyr Ser Thr Ser Asn Leu	
<u>CDR3</u>	
AAT TCT GGT GTC CCA TCA AGG TTC AGT GGC AGT GGG TCT GGG TCA GAT TAT TCT	72
Asn Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Asp Tyr Ser	
CTC ACC ATC AGC AGC CTA GAC TCT GAA GAT TTT GCA GAC TAT TAC TGT CTA CAG	90
Leu Thr Ile Ser Ser Leu Asp Ser Glu Asp Phe Ala Asp Tyr Tyr Cys Leu Gln	
<u>CDR3</u>	
CGT AAT GCG TAT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	107
Arg Asn Ala Tyr Pro Tyr Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys	

Figure 2

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODIES NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. ~~et al.~~ Serial No.: Not yet assigned Docket No.: 690022.527C2

Light chain

1	ASP	ILE	GLN	MET	5	THR	GLN	SER	PRO	SER	10	SER
11	LEU	SER	ALA	SER	15	VAL	GLY	ASP	ARG	VAL	20	THR
21	ILE	THR	CYS	ARG	25	ALA	SER	GLN	GLY	ILE	30	ARG
31	GLY	ASN	LEU	ASP	35	TRP	TYR	GLN	GLN	LYS	40	PRO
41	GLY	LYS	GLY	PRO	45	LYS	LEU	LEU	ILE	TYR	50	SER
51	THR	SER	ASN	LEU	55	ASN	SER	GLY	VAL	PRO	60	SER
61	ARG	PHE	SER	GLY	65	SER	GLY	SER	GLY	SER	70	ASP
71	TYR	THR	LEU	THR	75	ILE	SER	SER	LEU	GLN	80	PRO
81	GLU	ASP	PHE	ALA	85	THR	TYR	TYR	CYS	LEU	90	GLN
91	ARG	ASN	ALA	TYR	95	PRO	TYR	THR	PHE	GLY	100	GLN
101	GLY	THR	LYS	LEU	105	GLU	ILE	LYS				

The humanised sequence of NRX451 light chain, residue positions which differ between NR-LU-13 & NRX451-humanised are marked with bold type.

Figure 3

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN FOUND BY
ANTIBODIES NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. ~~et al.~~ Serial No.: Not yet assigned Docket No. 690022.527C2

Heavy chain											
1	VAL	GLN	LEU	5	VAL	GLN	SER	GLY	ALA	10 GLU	
11	VAL	LYS	LYS	PRO	15	GLY	ALA	SER	VAL	LYS	20 VAL
21	SER	CYS	LYS	ALA	25	SER	GLY	PHE	ASN	ILE	LYS
31	ASP	THR	TYR	MET	HIS	TRP	VAL	ARG	GLN	ALA	
41	PRO	GLY	GLN	GLY	45	LEU	GLN	TRP	MET	GLY	50 ARG
51	ILE	ASP	PRO	ALA	ASN	GLY	ASN	THR	LYS	CYS	
61	ASP	LEU	SER	PHE	65	GLN	GLY	ARG	VAL	THR	70 ILE
71	THR	ALA	ASP	THR	75	SER	ILE	ASN	THR	ALA	80 TYR
81	MET	GLU	LEU	SER	85	SER	LEU	ARG	SER	ASP	90 ASP
91	THR	ALA	VAL	TYR	95	TYR	CYS	SER	ARG	GLU	100 VAL
101	LEU	THR	GLY	THR	105	TRP	SER	LEU	ASP	TYR	110 TRP
111	GLY	GLN	GLY	THR	115	LEU	VAL	THR	VAL	SER	120 SER

The humanized sequence of NRX451 heavy chain, residue positions which differ between NR-LU-13 and NRX451-humanised are marked with bold type.

Figure 4

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN FOUND BY
ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Davies et al. Serial No.: Not yet assigned Docket No.: 690022.527C2.

Alignment of the Light Chain Variable Regions of NR-LU-13 (top) and humanized NRX451 (bottom).

DIQMISSPSSMFASLGDRVSLSC RASQGIRGNLD WYQQKPGGTIKLLIY STSNLNS

DIQMTQSPSSLSASVGDRVITIC RASQGIRGNLD WYQQKPGKGPKLLIY STSNLNS
CDR1 CDR2

GVPSRFSGSGSGSDYSLTISSLESEDFA~~D~~YYC LQRNAYPYTF GGGTKLEIK

GVPSRFSGSGSGSDYTLTISSLQPEDFA~~T~~YYC LQRNAYPYTF GQG~~T~~KLEIK
CDR3

Alignment of the Heavy Chain Variable Regions of NR-LU-13 (top) and humanized NRX 451 (bottom)

EVQLQQSGAELVKPGASVRLSCTASGFNIK DTYME WVIERPEQGLEWIG

QVQLVQSGAEVKPGASVKVSCKASGFNIK DTYME WVRQAPGQGLQWMG
CDR1

RIDPANGNTK CDPKFQGKATITADTSSNTAYLQLSSLTSEDTAVYYCS

RIDPANGNTK CDLSFQGRVTITADTSINTAYMELSSLRSDDTA~~V~~YYCS
CDR2

REVLTGTVSLDY WGQGTSVTVSS

REVLTGTVSLDY WGQGTLVTVSS
CDR3

Figure 5

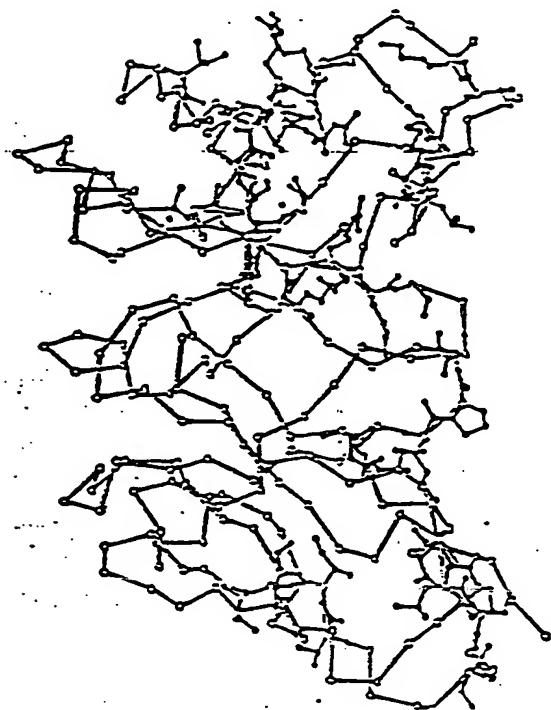
Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN FOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Davies et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

A



B

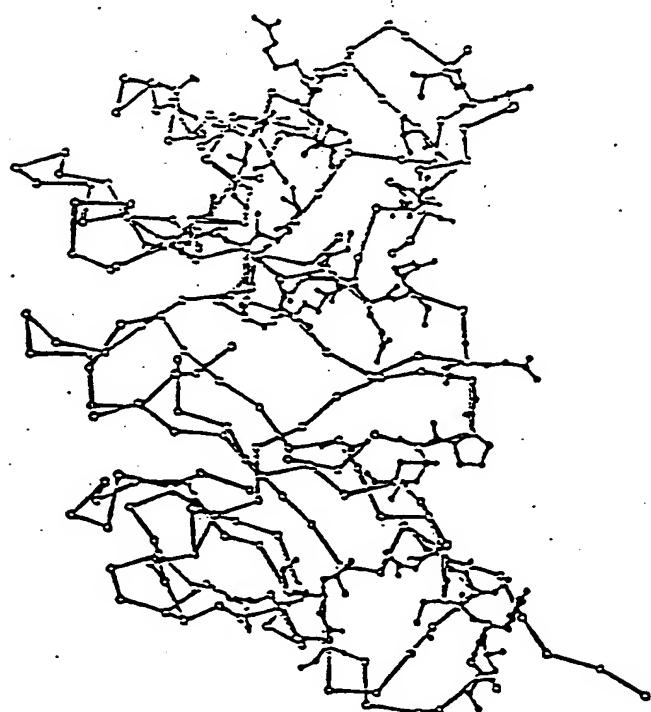


Figure 6

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN FOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. ~~Coates~~ et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

Same frequencies but matching with human sequences. Only one occurrence of Asp at position 182 is found and no occurrences of Cys at position 181.

RES	181	182
A	-	0.48
R	-	0.02
N	0.01	0.18
D	0.00	0.00
C	0.00	0.00
Q	0.00	-
E	-	-
G	0.00	0.01
H	0.00	-
I	-	0.00
L	-	0.00
K	0.00	0.00
M	-	-
F	0.03	-
P	0.00	0.01
S	0.01	0.23
T	-	0.02
W	0.00	-
Y	0.91	-
V	0.00	0.02
X	0.01	0.02
O	-	-
-	-	-
Z	-	-
B	-	0.00
Total	1.00	1.00

Figure 7A

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. ~~Charles~~ et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

Sequence positions 50 and 183 are structural mutations within 5 Å of the CDR's. Frequency of residue types at these positions are identical.

Position 50 (153 human lambda sequences)

RES	50
A	-
R	-
N	-
D	-
C	-
Q	-
E	-
G	-
H	-
I	0.00
L	-
K	-
M	0.00
F	-
P	0.93
S	-
T	-
W	-
Y	-
V	-
X	0.06
O	-
-	-
Z	-
B	-
Total	1.00

Figure 7B

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Davies et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

Position 50 (279 human kappa sequences)

RES	50
A	0.00
R	-
N	-
D	-
C	-
Q	-
E	-
G	-
H	-
I	0.00
L	0.00
K	-
M	-
F	-
P	-
S	-
T	-
W	-
Y	-
V	-
X	-
O	0.03
-	-
Z	-
B	-
Total	1.00

Figure 7C

Position 50 is highly conserved in all the sequences but proline can be exchanged by Ile or Leu. The framework used for the light chain (6fab) does have an Ile at this position. If this position is compared to other structures the backbone torsions are the same for structures with a Pro and an Ile at this position.

Position 183 (561 human sequences)

RES	183
A	0.06
R	-
N	0.00
D	0.21
C	-
Q	0.15
E	0.01
G	0.01
H	-
I	0.00
L	0.00
K	0.00
M	-
F	0.00
P	0.40
S	0.01
T	0.01
W	-
Y	0.00
V	0.08
X	0.02
O	-
-	-
Z	-
B	0.00
Total	1.00

Figure 7D

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Carver et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

Position 183 (1210 mouse sequences)

RES	183
A	0.16
R	0.00
N	0.00
D	0.13
C	-
Q	0.16
E	0.25
G	0.02
H	0.00
I	-
L	-
K	0.00
M	-
F	-
P	0.17
S	0.08
T	0.00
W	-
Y	-
V	0.00
X	0.02
O	-
-	-
Z	-
B	-
Total	1.00

Leu is seen in human sequences at this position, but never in murine sequences, for both human and murine Sequences P is the most frequently occurring residue at position 183.

Figure 7E

Comments for pcDNAs:**5446 nucleotides**

CMV promoter: bases 209-883

T7 promoter: bases 884-882

Polylinker: bases 889-994

Sp6 promoter: bases 999-1018

BGH poly A: bases 1018-1249

SV40 promoter: bases 1790-2115

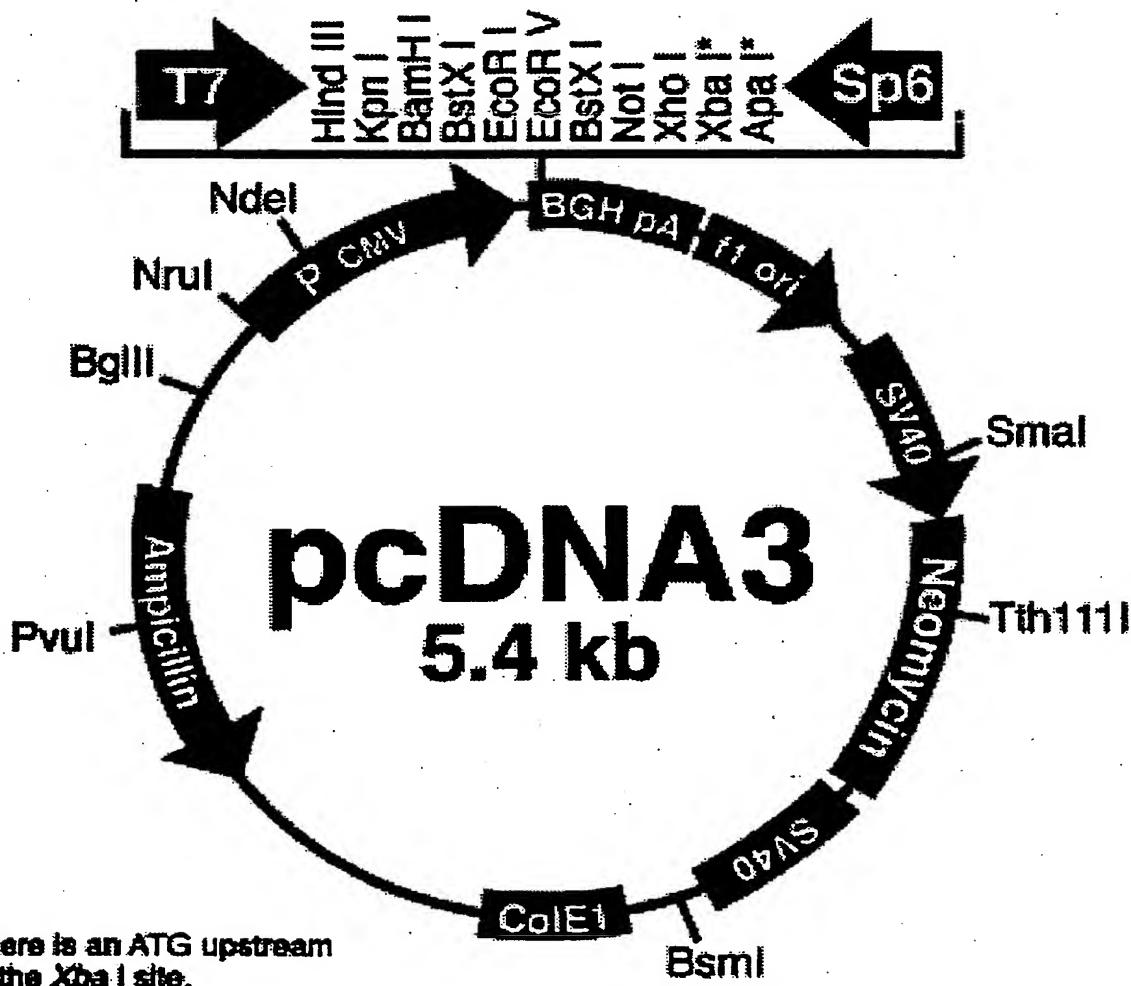
SV40 origin of replication: bases 1984-2069

Neomycin ORF: bases 2151-2945

SV40 poly A: bases 3000-3372

ColE1 origin: bases 3632-4305

Ampicillin ORF: bases 4450-5310

**Figure 8**

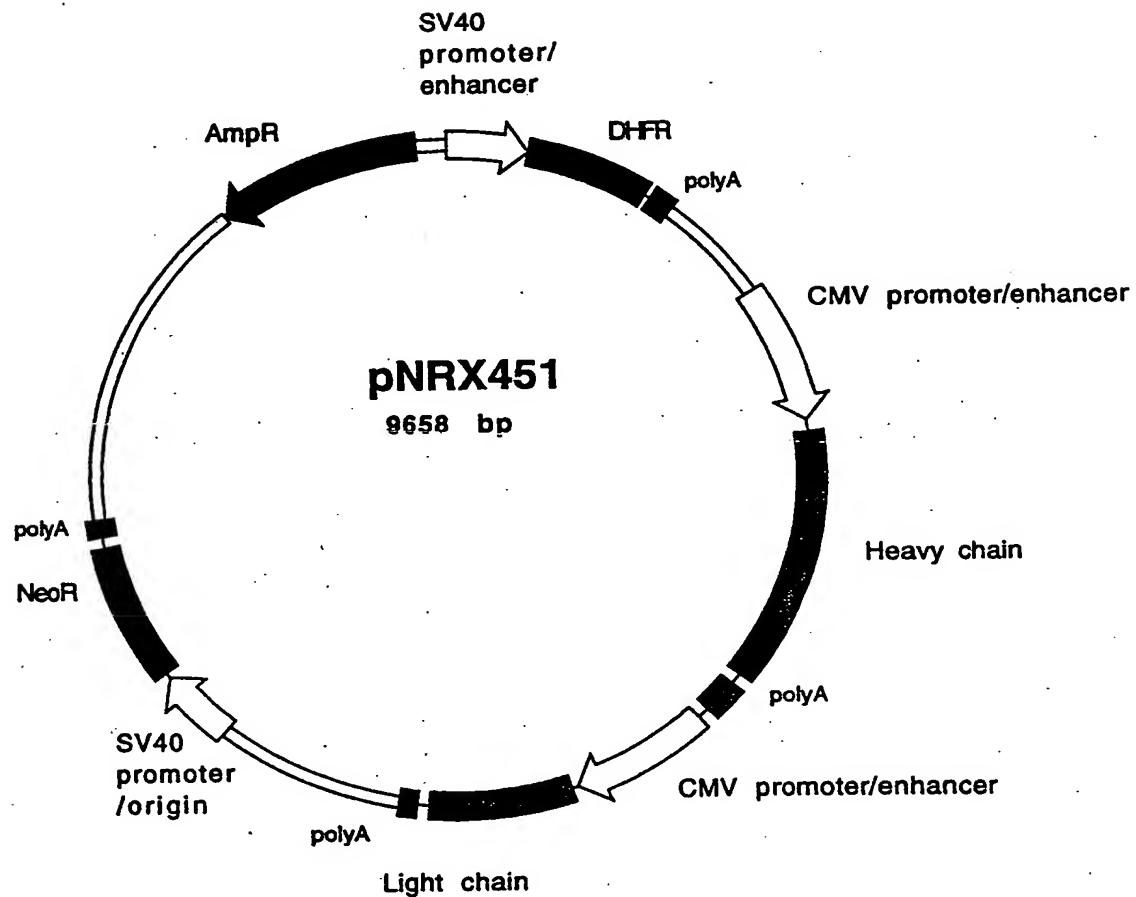


Figure 9

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

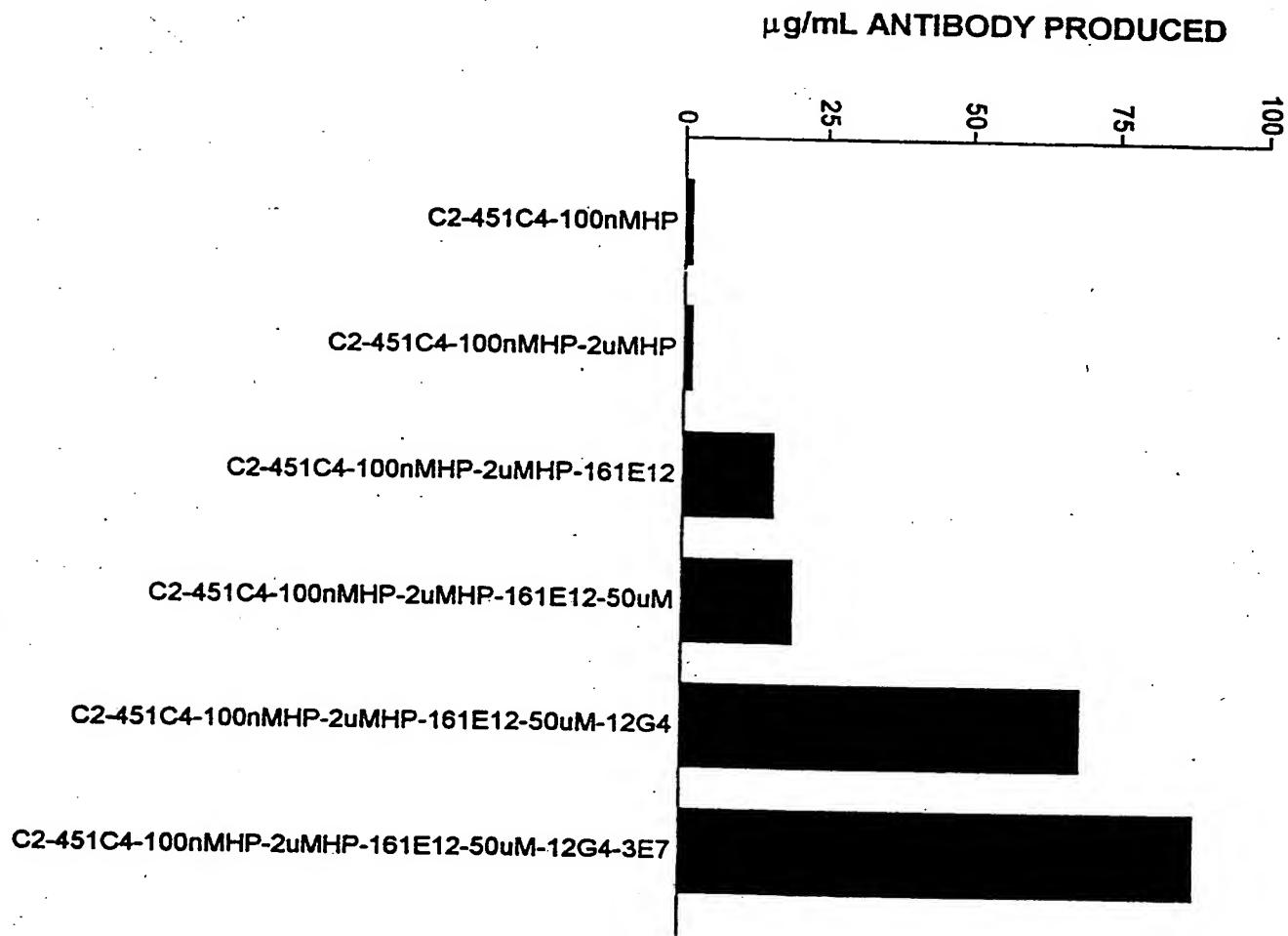


Figure 10

POOL of CLONE

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY

ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Davies et al. Serial No.: Not yet assigned Docket No. 690022.527C2

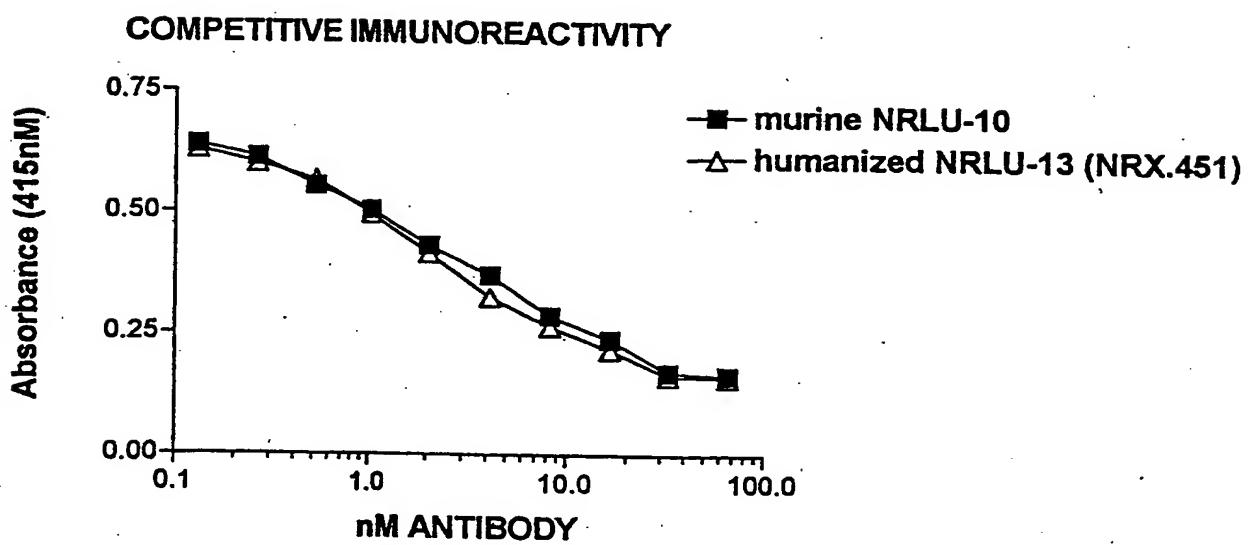


Figure 11

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY
ANTIBODY NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Davies et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

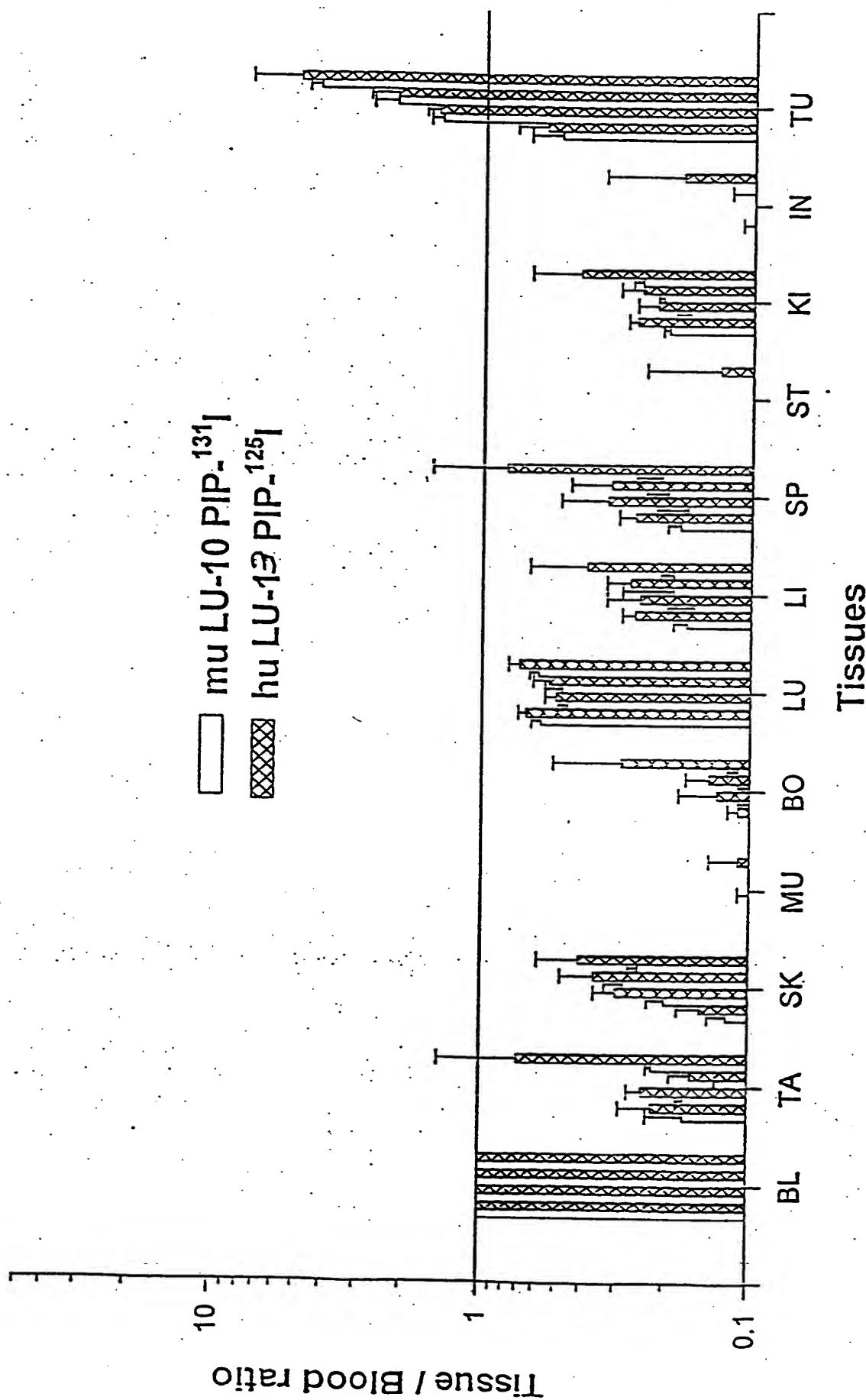


Figure 12

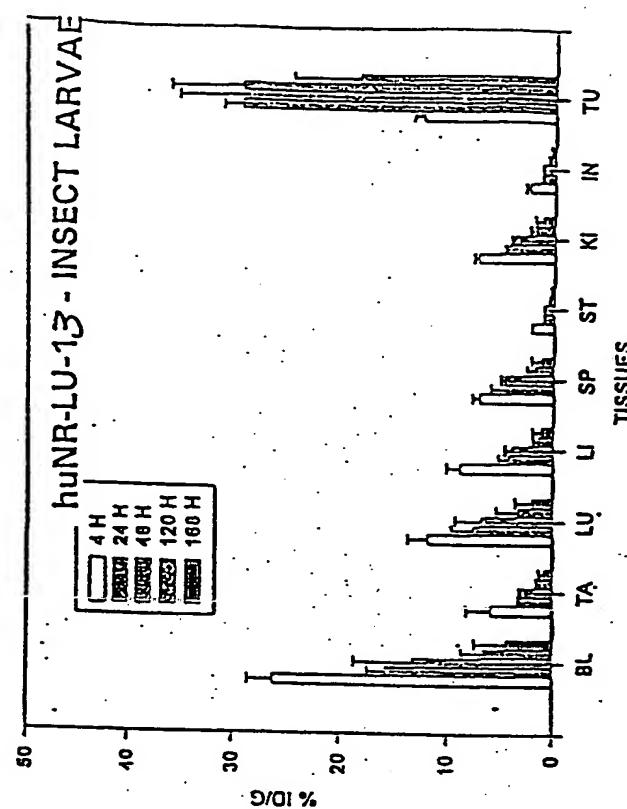
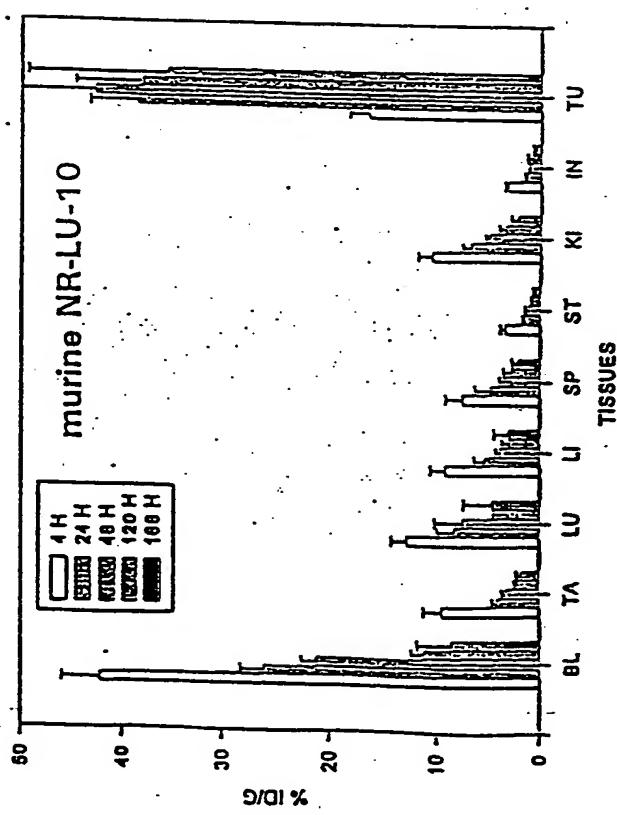
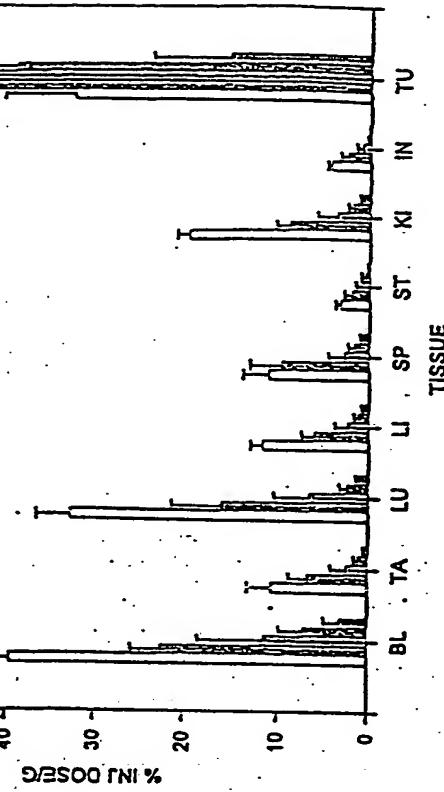
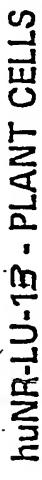
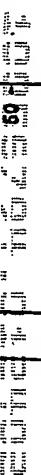
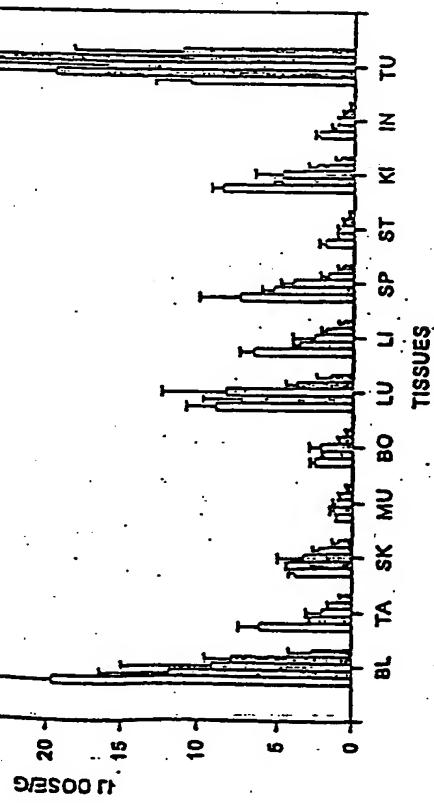


Figure 13

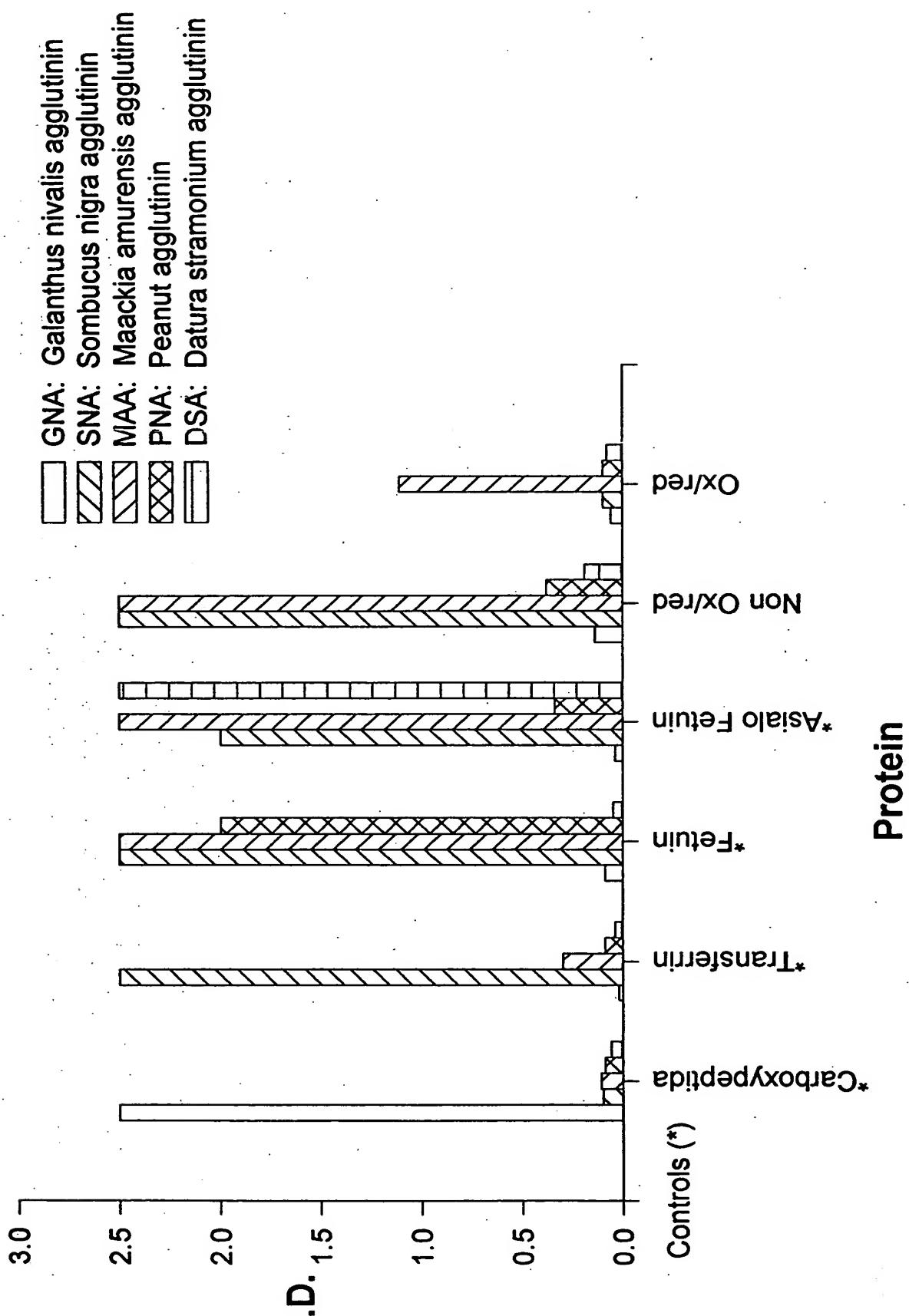


Figure 14

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN EXPRESSED BY

ANTIBODY 4F2-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

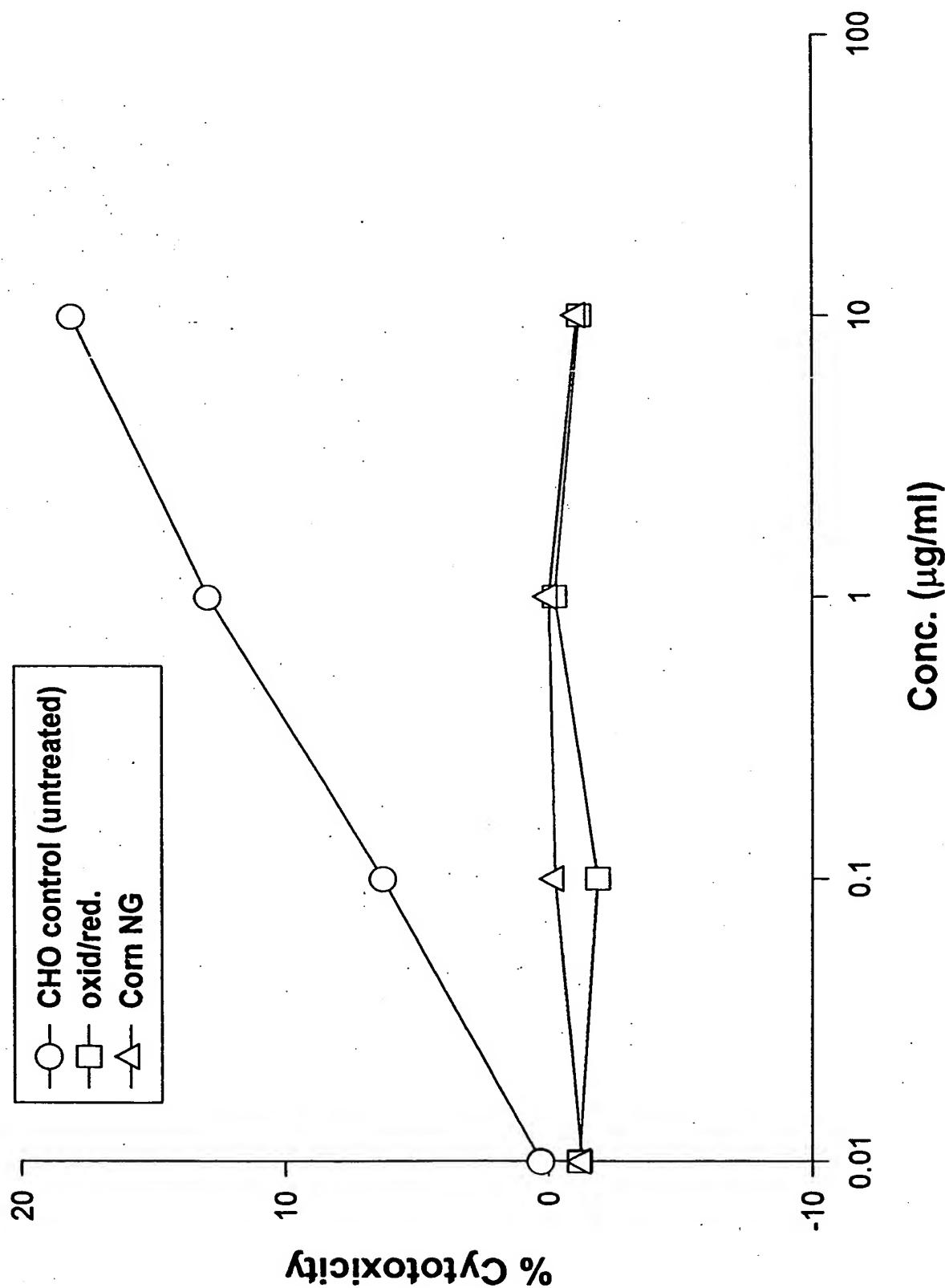


Figure 15a

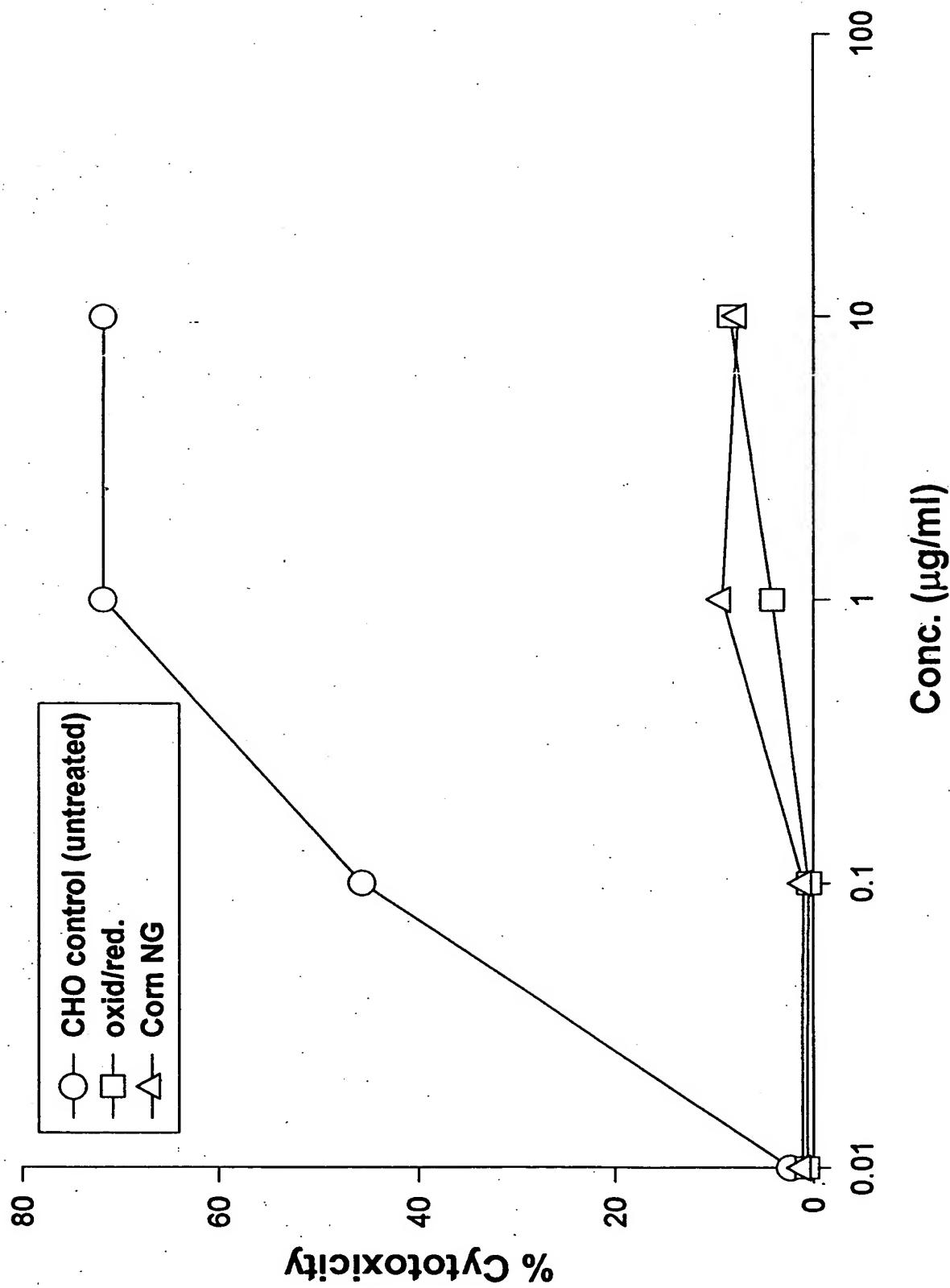


Figure 15b

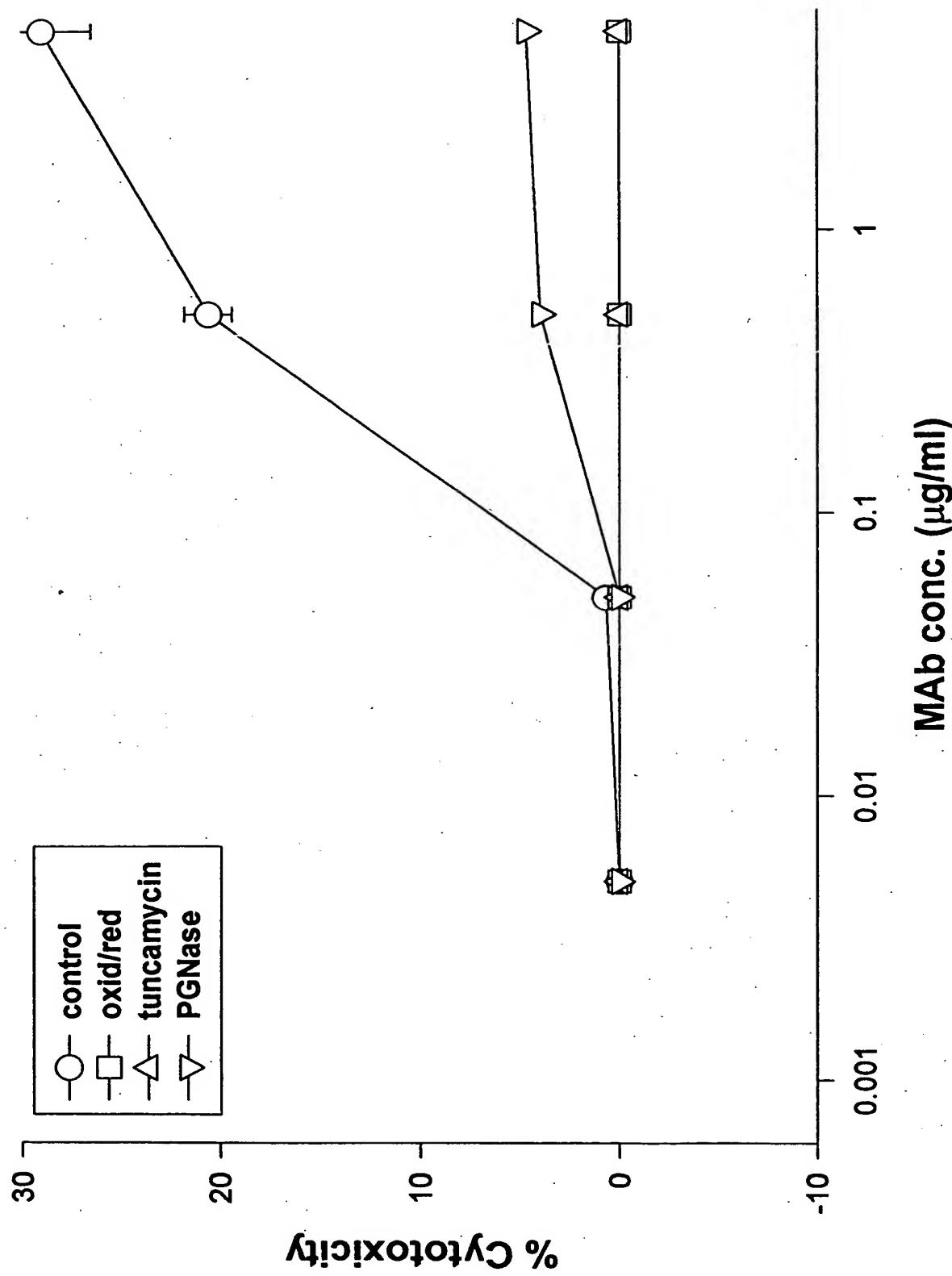


Figure 15c

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY
ANTIBODY 9R-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

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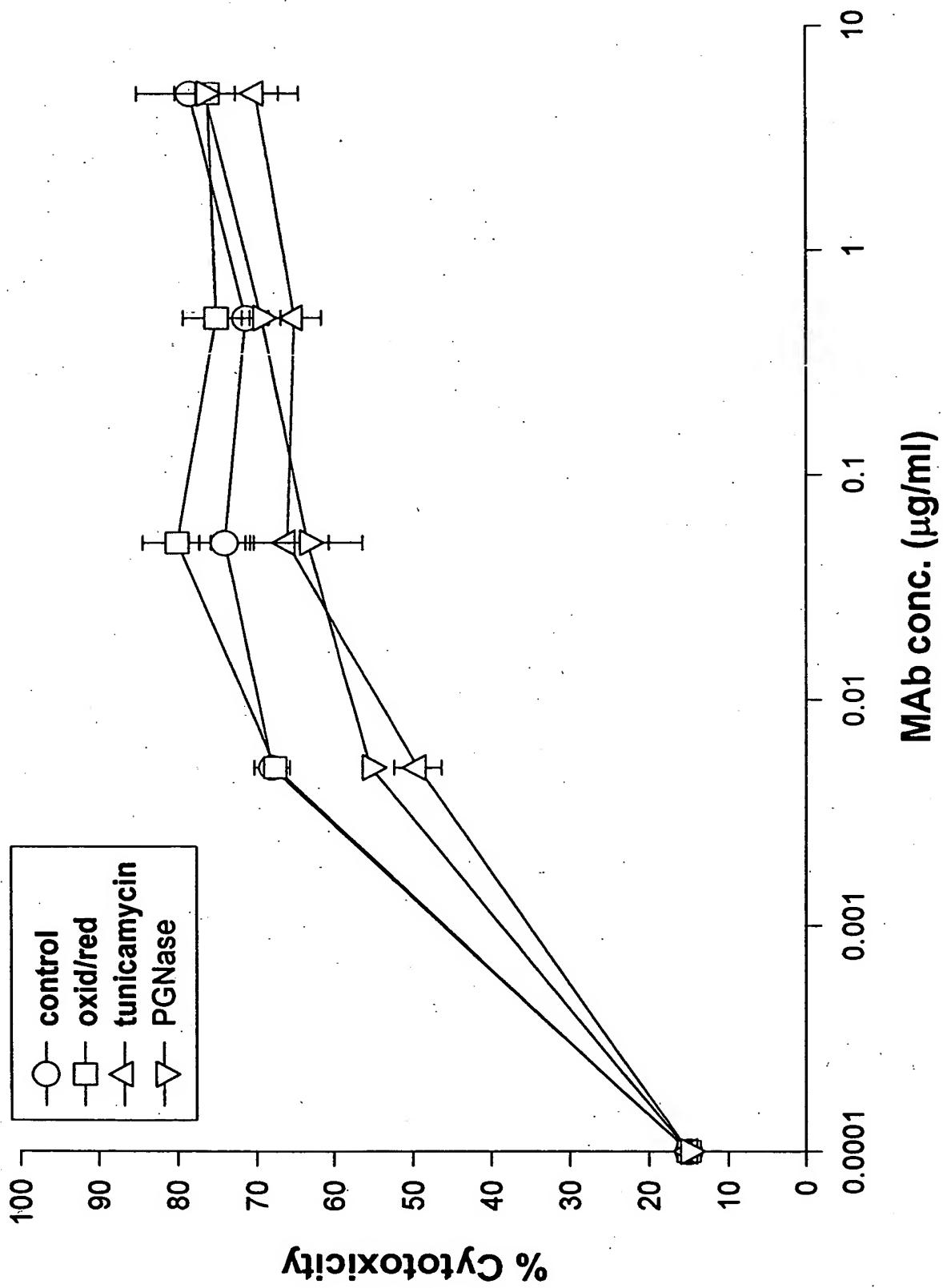


Figure 15d

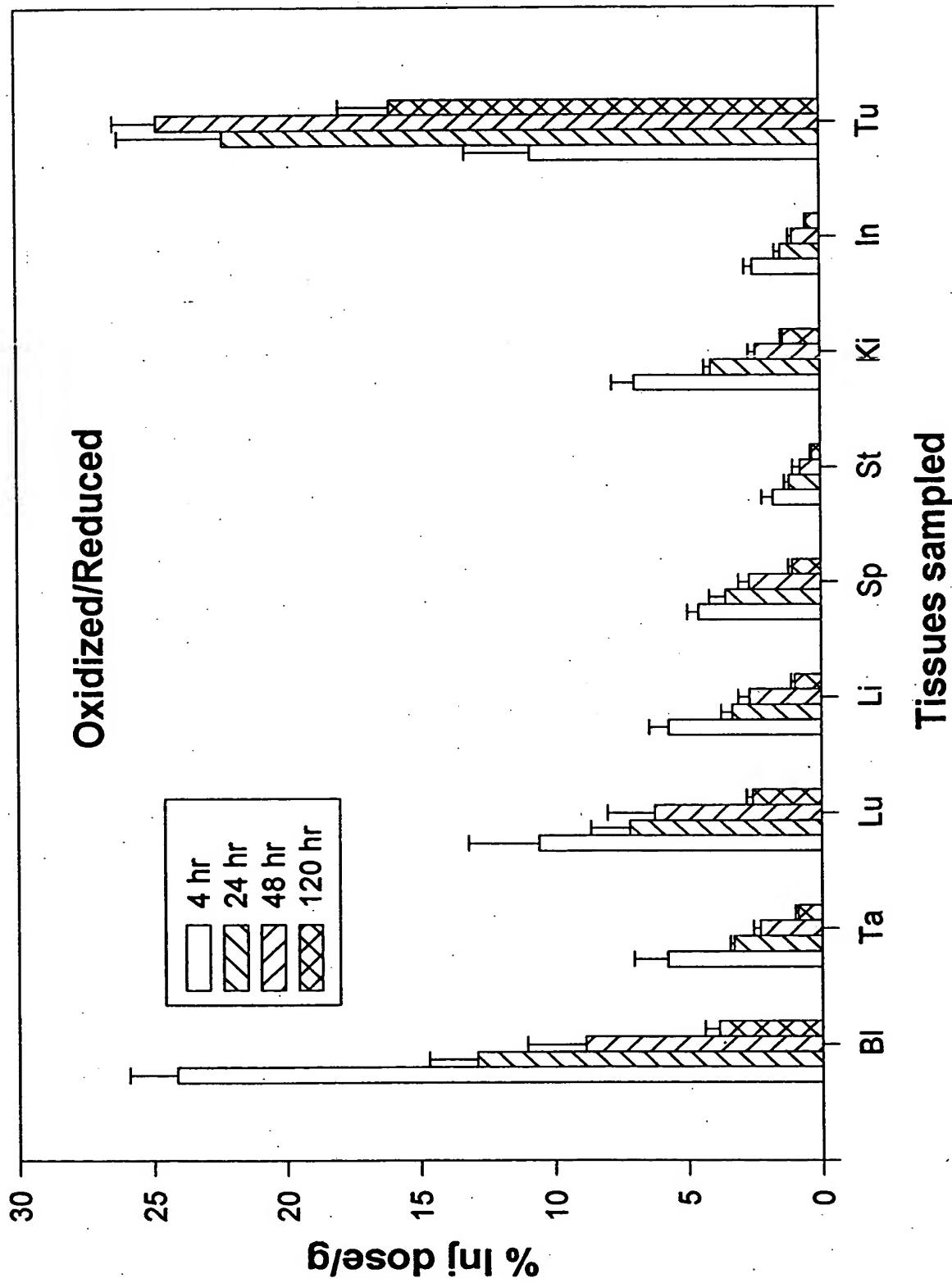


Figure 16a

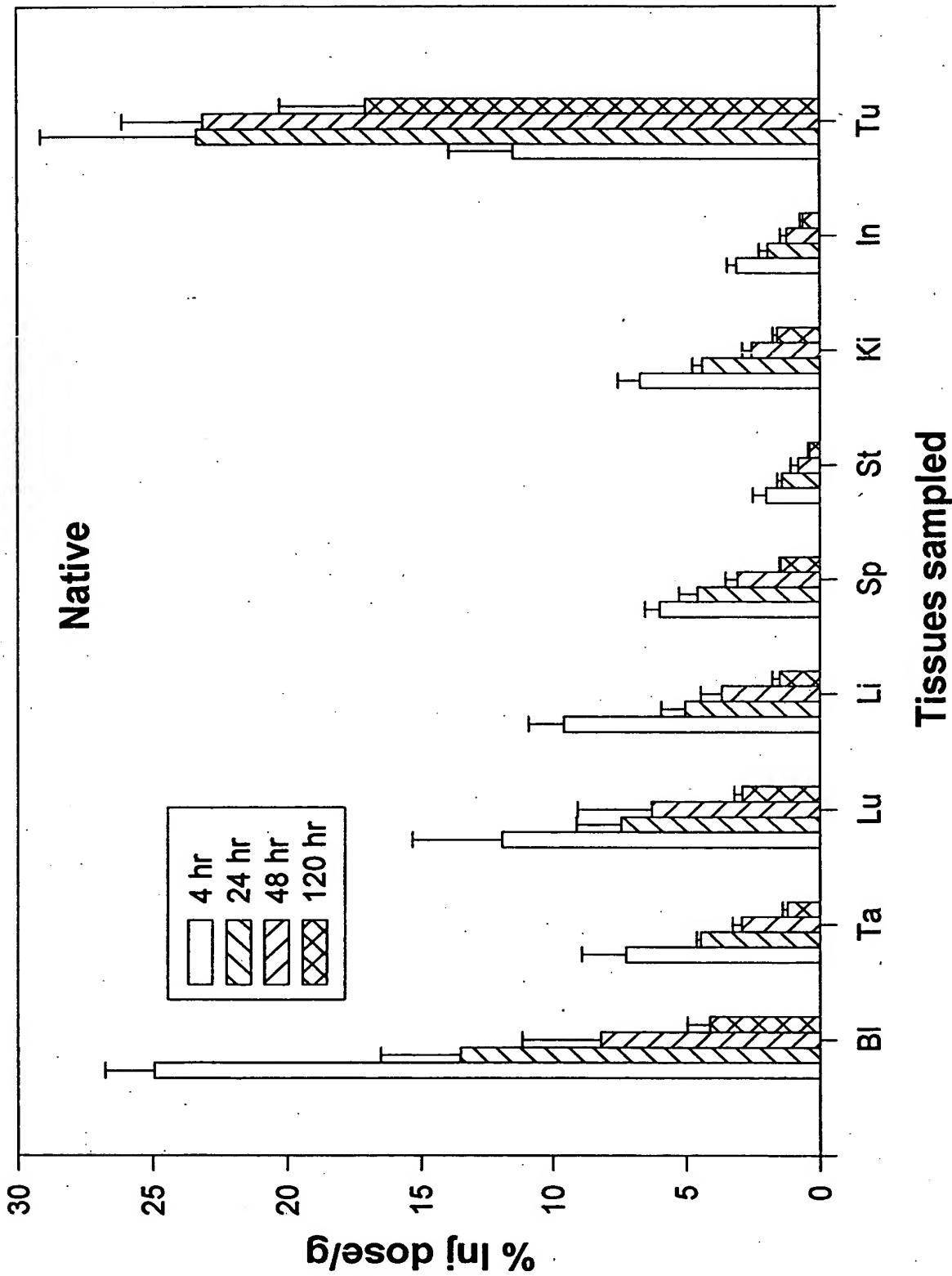


Figure 16b

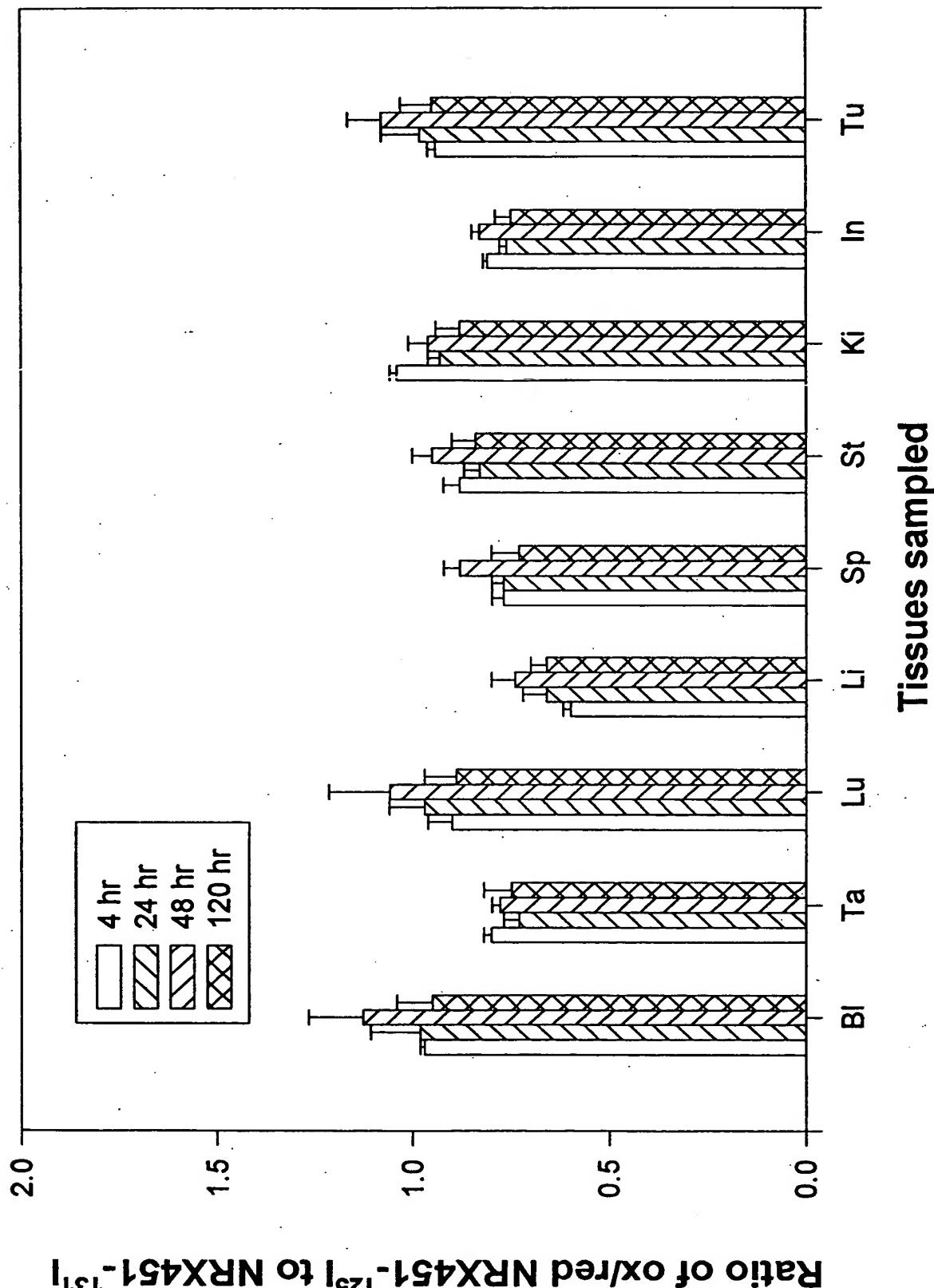


Figure 16c

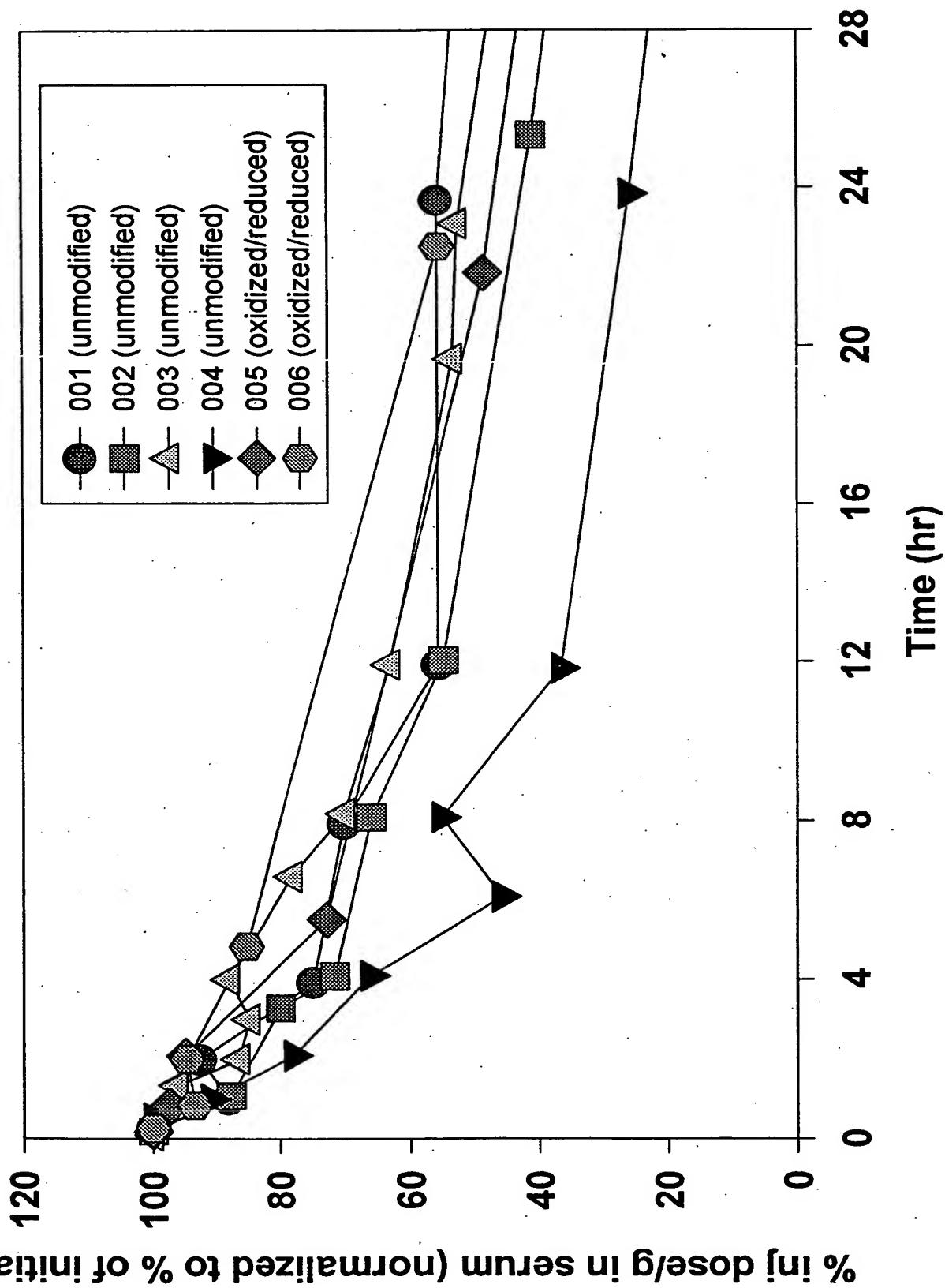


Figure 17

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUND BY
ANTIBODY 4R-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

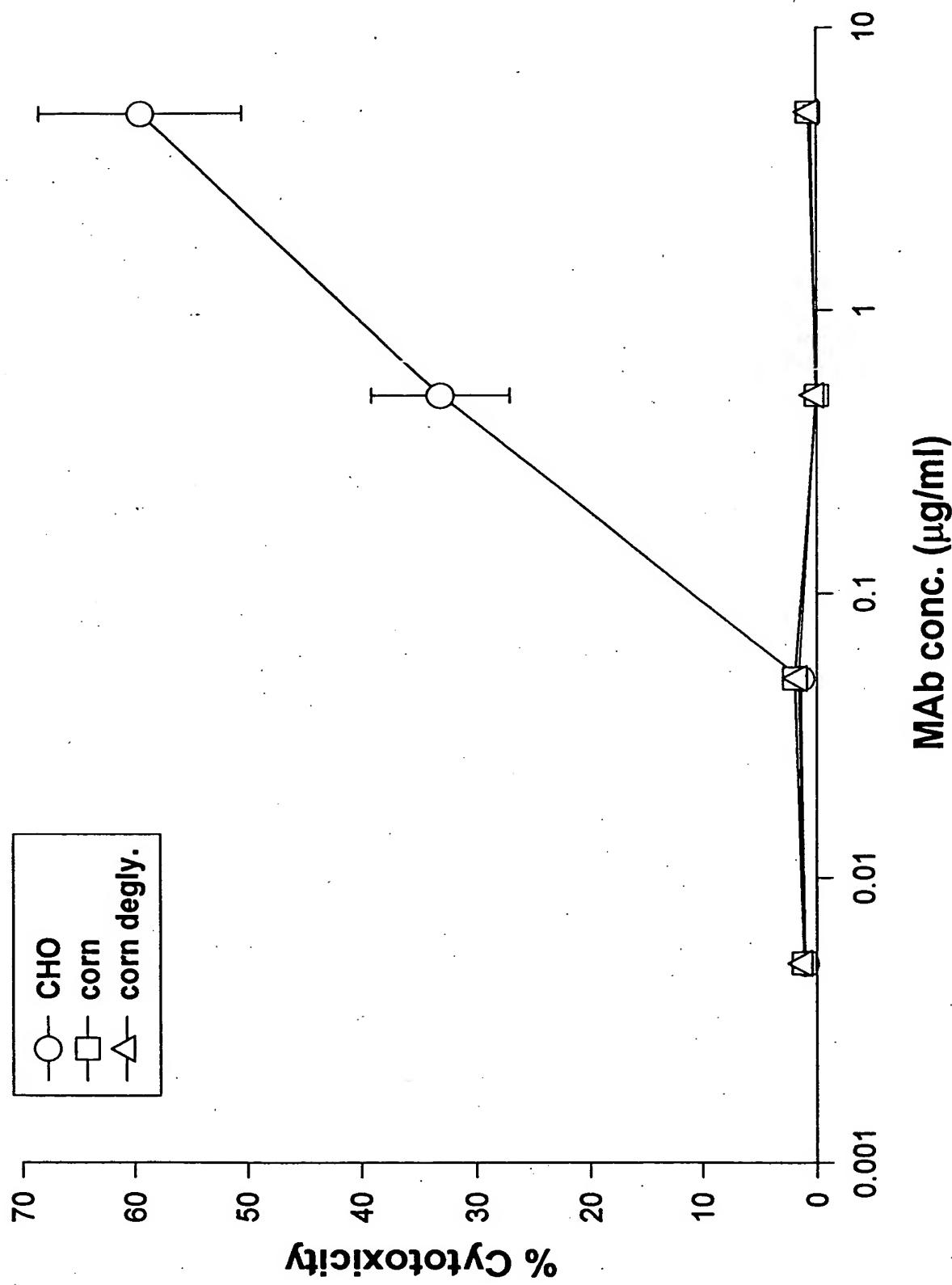


Figure 18

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN FOUND BY

ANTIBODY JR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

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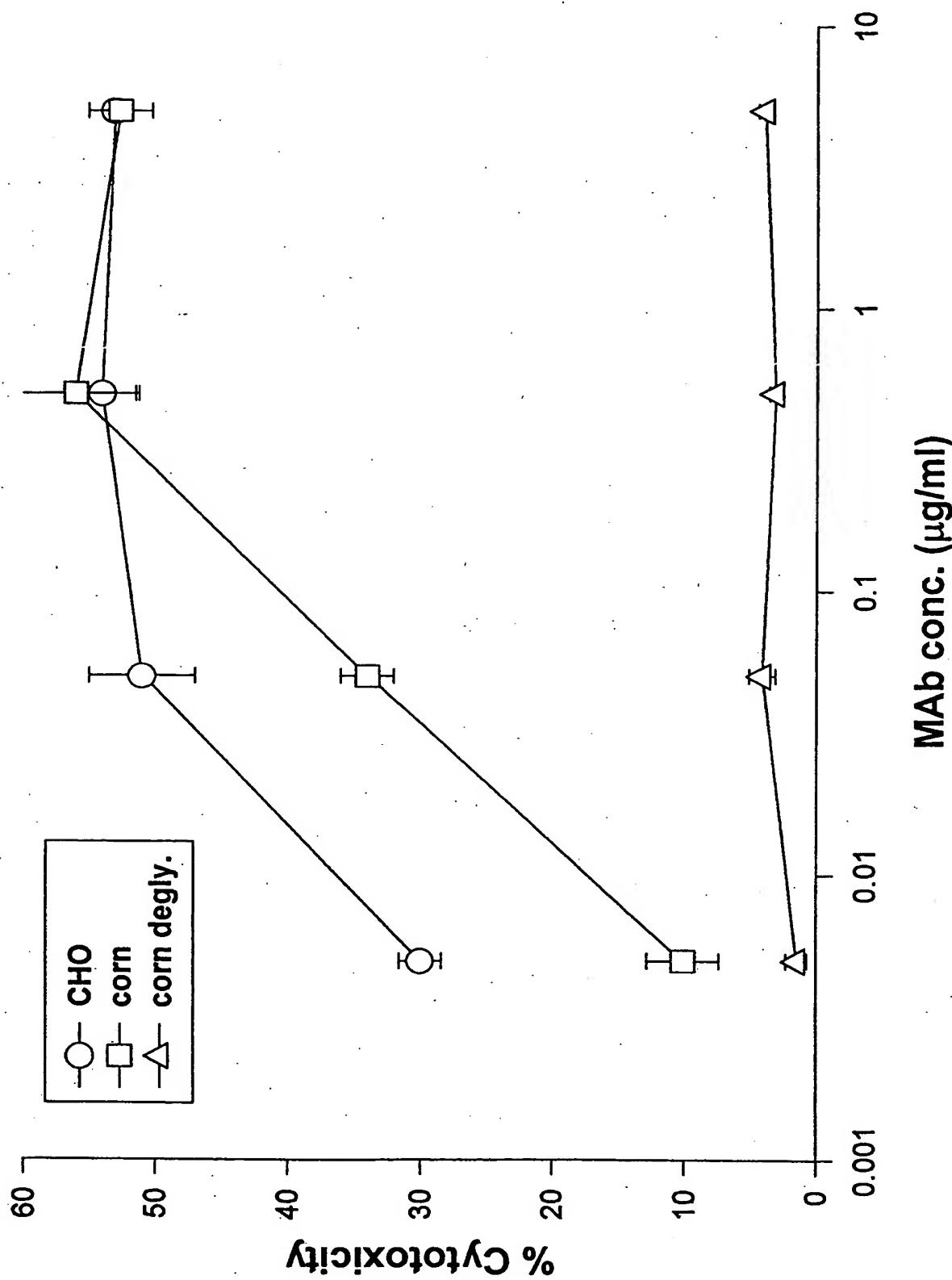


Figure 19

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOULD BY
ANTIBODIES NR-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Graves et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

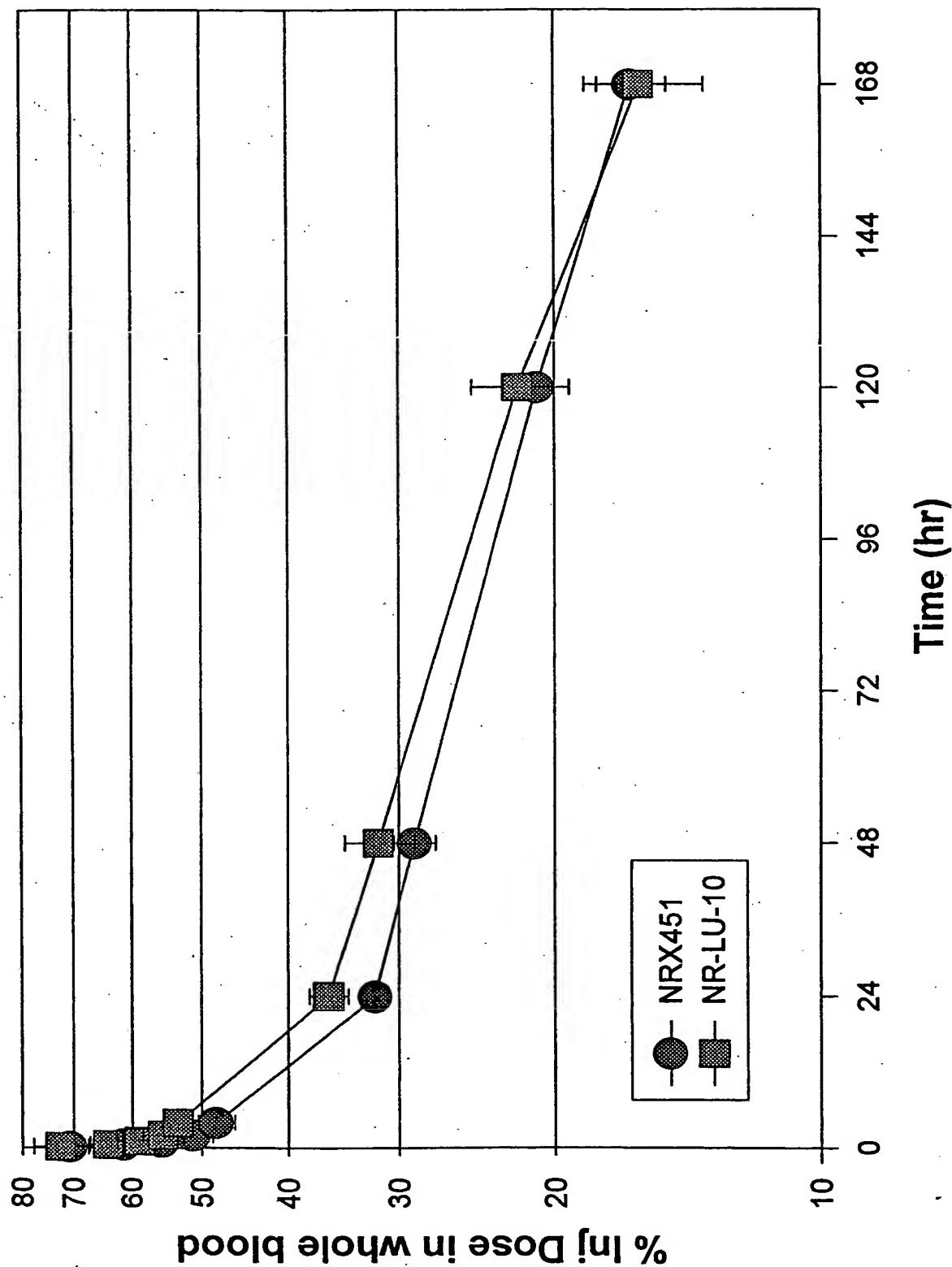


Figure 20

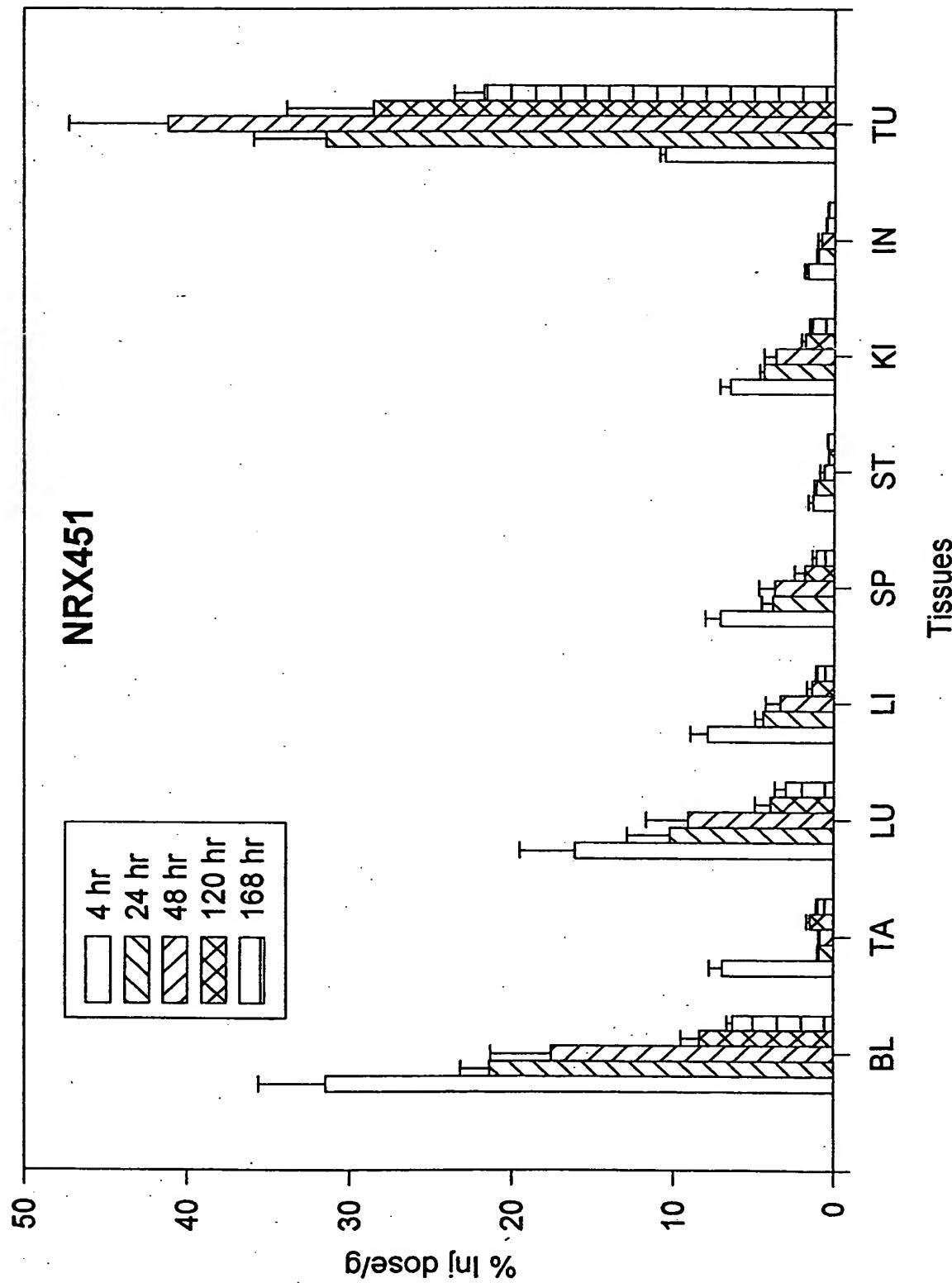


Figure 21a

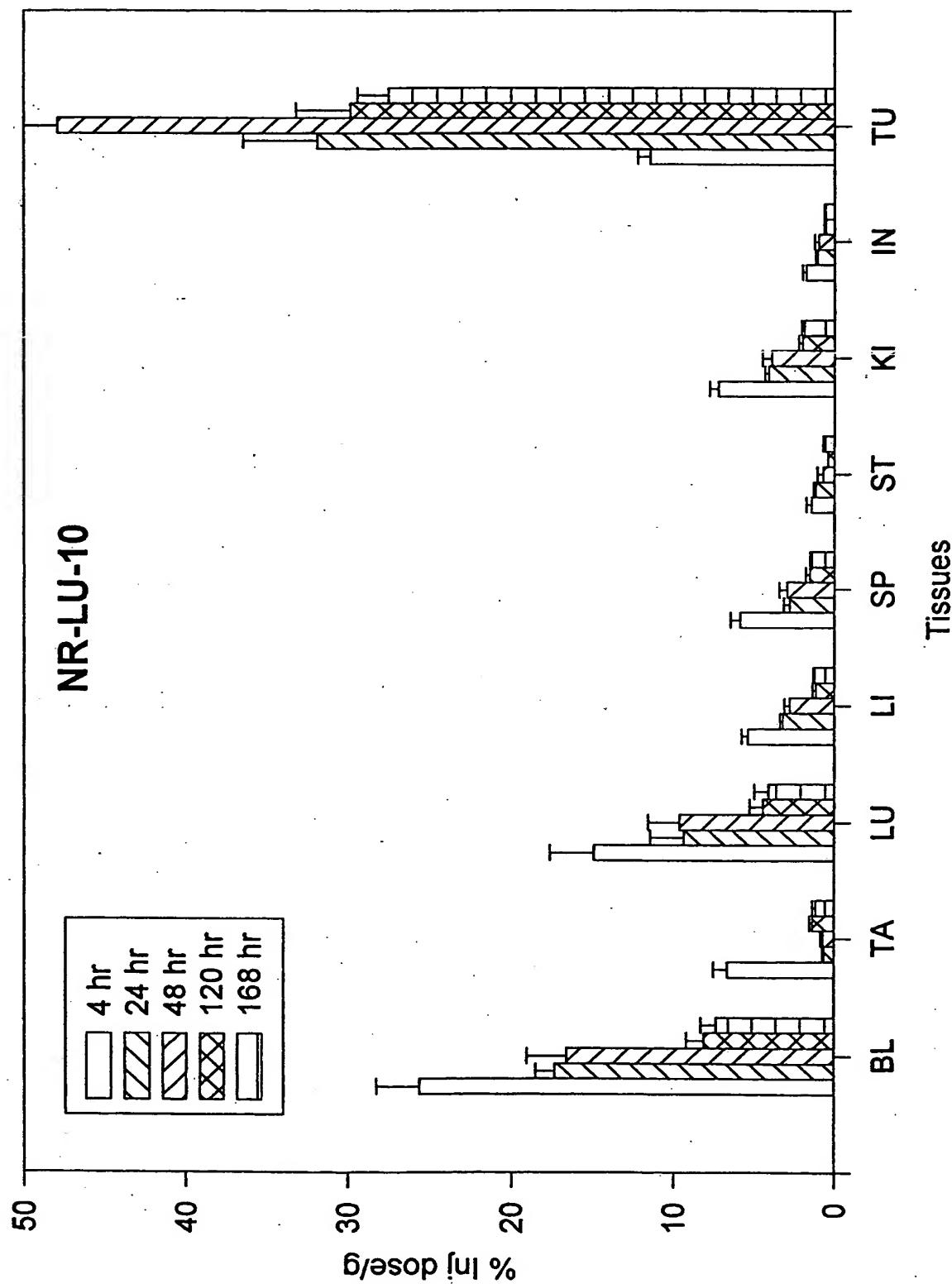


Figure 21b

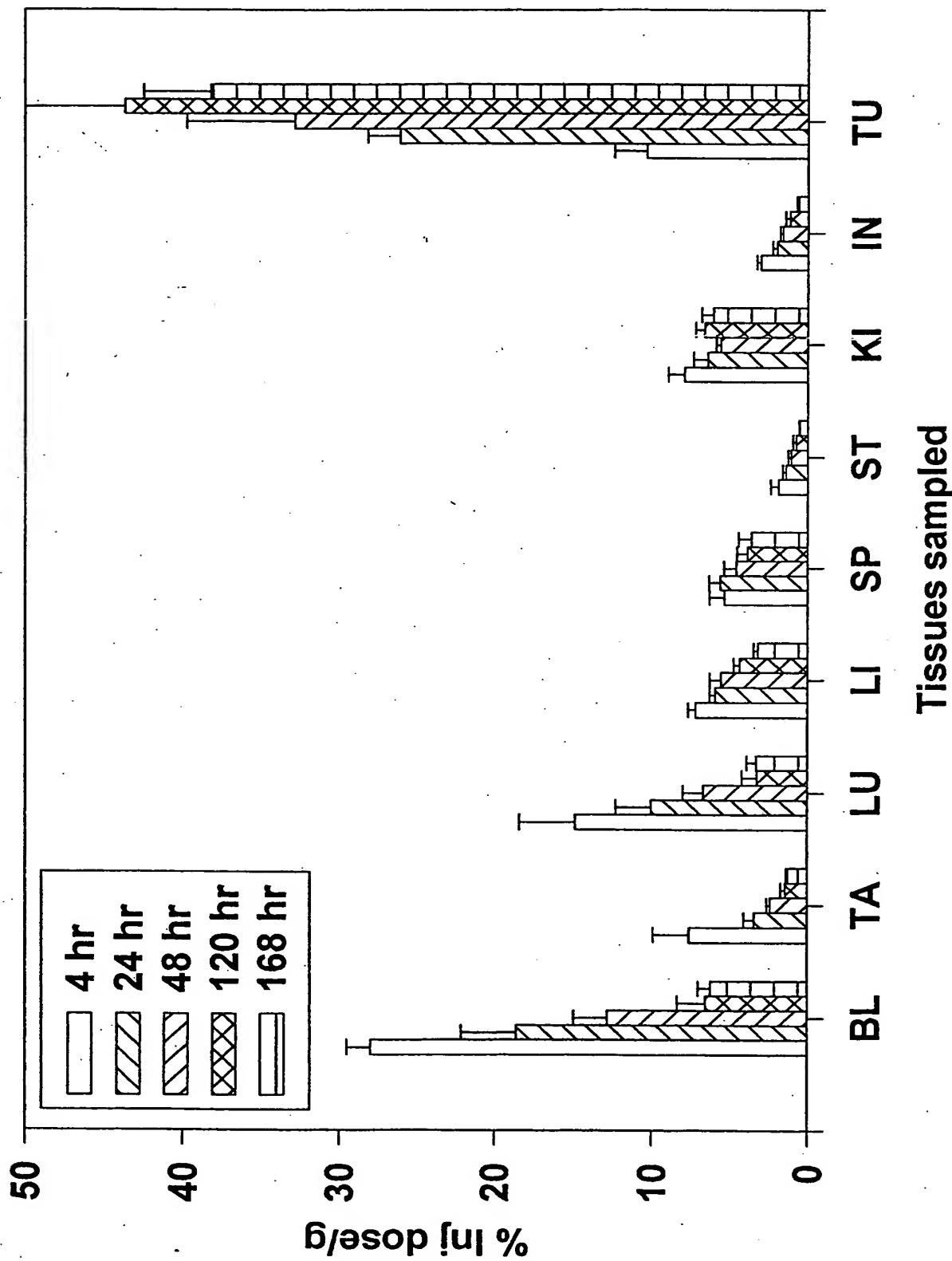


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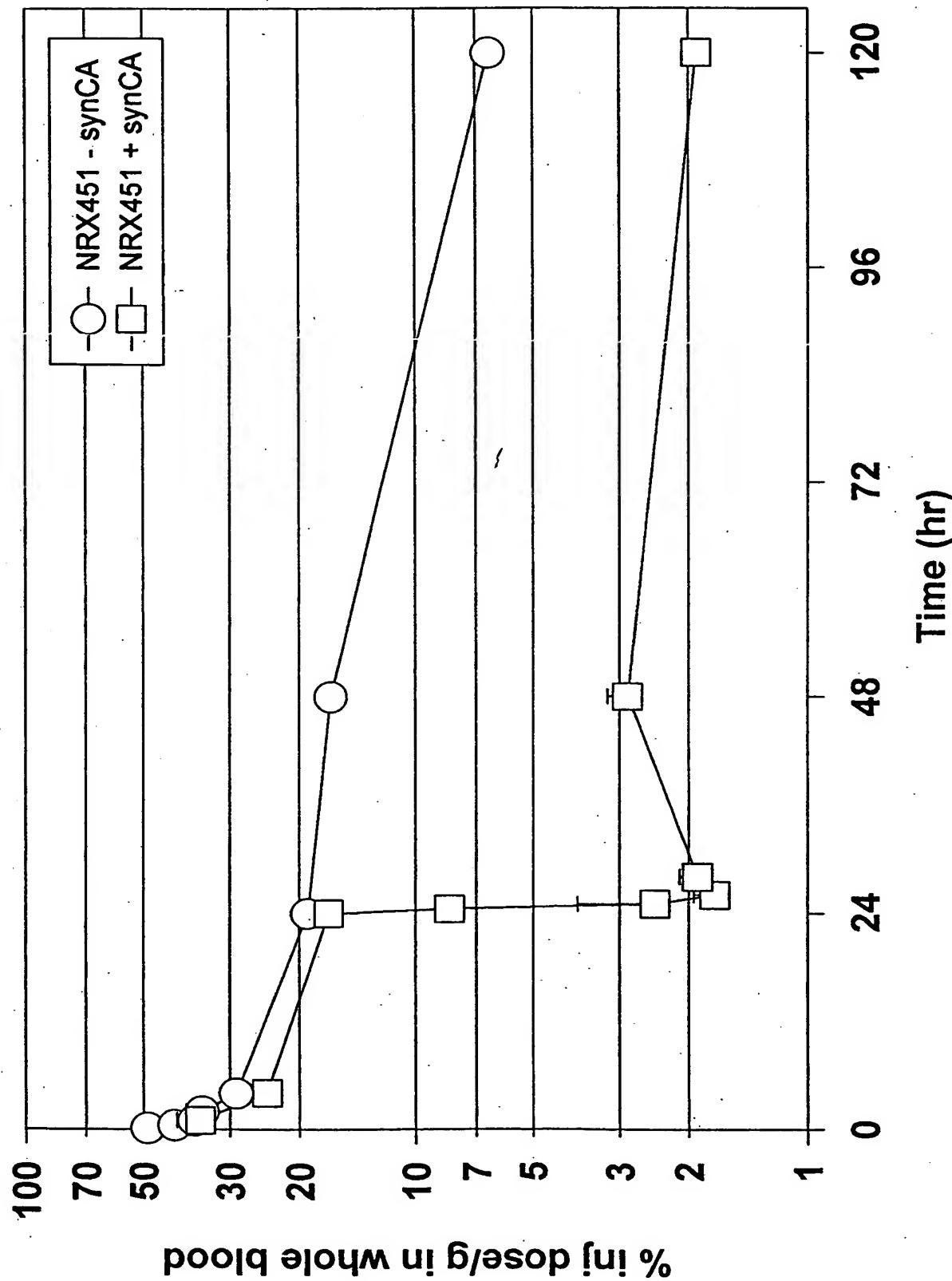


Figure 23

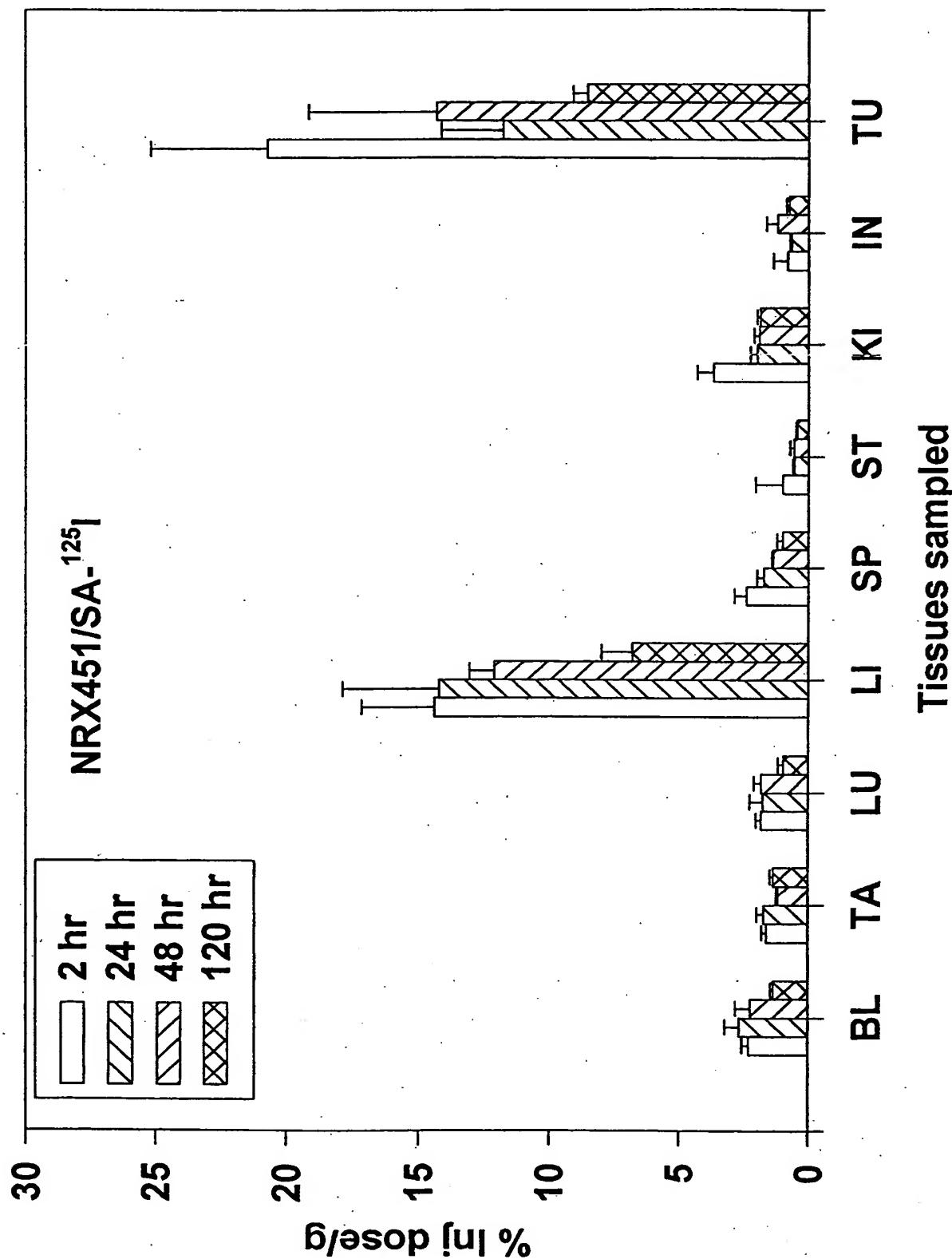


Figure 24a

Express Mail No.: EV064839733US

Title: HUMANIZED ANTIBODIES THAT BIND TO THE ANTIGEN BOUGHT BY
ANTIBODIES R-LU-13 AND THEIR USE IN PRETARGETING METHODS

Inventors: Scott S. Gaines et al. Serial No.: Not yet assigned Docket No.: 690022.527C2

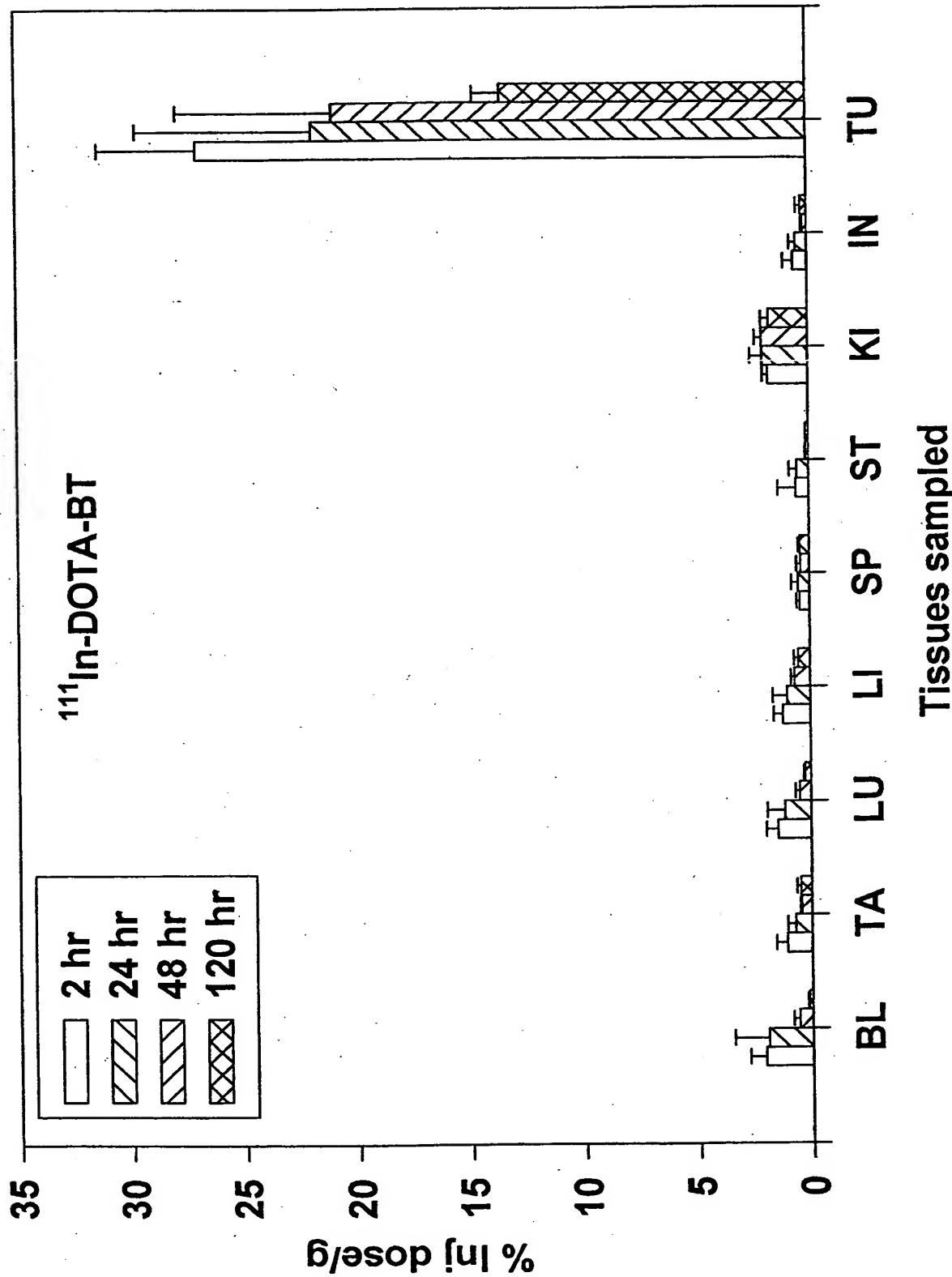


Figure 24b